

***Remarks***

Reconsideration of this Application and entry of the Amendments are respectfully requested.

Claims 1 and 41 are sought to be amended. Support for the amendments can be found, *inter alia*, in paragraphs 0026 and 0027 of the captioned application, and throughout the specification and claims as originally filed. These changes are believed to introduce no new matter, and their entry is respectfully requested.

Upon entry of the foregoing amendment, claims 1-41 are pending in the application, with 1, 9, 17, 23-25 and 29-41 being the independent claims. Claims 10-40 have been withdrawn from further consideration as being drawn to non-elected inventions. Based on the above amendment and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding rejections and that they be withdrawn.

***Rejections under 35 U.S.C. § 112, First Paragraph***

Claims 1-9 and 41 remain rejected under 35 U.S.C. § 112, first paragraph. (Office Action dated July 2, 2004, Section 2.) Applicants respectfully traverse this rejection.

The Examiner stated that, despite Applicants' argument:

... that they have enabled the full scope of the claims with regard to identifying agents capable of treating all neurodegenerative diseases associated with neuronal cell death, Applicants would need to demonstrate that the identified agents are, in fact, able to treat the claimed diseases. To obviate this part of the rejection. . .the claims should be amended to recite "a method of identifying an agent which is a candidate for the treatment of a neurodegenerative disease". . .

(Office Action date July 2, 2004, at page 2.) Applicants respectfully disagree.

As pointed out at page 16 of the Reply dated April 27, 2004, the claims being rejected are drawn to methods of identifying agents, not to the agents themselves. However, solely in an effort to facilitate prosecution and without acquiescing in the propriety of the rejection, Applicants have amended independent claims 1 and 41 to recite "a candidate agent."

The Examiner also asserted that "the claim should recite whether the potentiation, or the inhibition of the potentiation of CCE would be the desired endpoint for the treatment of a neurodegenerative disease." *Id.* Solely in an effort to facilitate prosecution and without acquiescing in the propriety of the rejection, Applicants have amended claims 1 and 41 to recite "identifying said agent that potentiates CCE as a candidate agent for treating a neurodegenerative disease." Applicants reserve the right to file a continuing or divisional application with claims directed to the identification of agents that "inhibit potentiation of CCE."

The Examiner also stated that "Applicants have not taught which animal studies are to be used to measure CCE, and what endpoints in these animal studies will be used to determine a potentiation of CCE in these animals." (Office Action of July 2, 2004, at page 3.) For purposes of clarification, Applicants have amended independent claims 1 and 41 to recite "testing said identified candidate agent in animal studies for toxicity or stability." Applicants note that the testing step (d) recited in the present claims is not directed to measuring CCE, as suggested by the Examiner. Rather, the testing in animal studies is performed to determine the toxicity or stability of the identified candidate agent. That is not to say that the steps of assaying for CCE activity could not be performed in an animal; however, testing step (d) of the present claims does not specify

measuring CCE. The types of animal studies that can be used for testing toxicity or stability of compounds can be readily determined by one of ordinary skill in the art without undue experimentation.

Accordingly, the Examiner's grounds of rejection of claims 1-9 and 41 under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement have been rendered moot. Applicants, therefore, respectfully request the Examiner to reconsider and withdraw this rejection.

In Section 3 of the Office Action dated July 2, 2004, the Examiner maintained the rejection of claims 1-9 and 41 under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. (See Office Action dated December 31, 2003, at page 3.) In particular, the Examiner alleged that these claims contain subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s) at the time the application was filed, had possession of the claimed invention). *Id.* Applicants respectfully traverse this rejection.

The Examiner asserted that he "cannot find support for methods of screening compounds which are able to treat diseases associated with neuronal cell death. This is a new matter rejection." *Id.* (emphasis omitted). Further, according to the Examiner, "it appears that the specification would imply that the neuronal cell death would be due to apoptosis only." (Office Action dated July 2, 2004, at page 3.) Applicants respectfully disagree with these assertions. One of ordinary skill in the art would have known that the death of neuronal cells in neurodegenerative diseases could result from a mechanism other than apoptosis. However, solely in an effort to facilitate prosecution and without acquiescing in the propriety of the rejection, Applicants have amended independent

claims 1 and 41 to recite "characterized by symptoms comprising amyloid aggregation or apoptotic neuronal cell death." Accordingly, the Examiner's grounds of rejection of claims 1-9 and 41 under 35 U.S.C. § 112, first paragraph, as allegedly adding new matter have been rendered moot. Applicants, therefore, respectfully request the Examiner to reconsider and withdraw this rejection.

***Rejections under 35 U.S.C. § 112, Second Paragraph***

Claims 1-9 and 41 were rejected under 35 U.S.C. § 112, second paragraph, as allegedly "being incomplete for omitting essential steps, such omission amounting to a gap between the steps." (Office Action dated July 2, 2004, Section 4.) Applicants respectfully traverse this rejection.

Specifically, the Examiner asserted that:

[t]he omitted steps are: a conclusion step reciting whether the potentiation, or the inhibition of the potentiation of CCE would be the desired endpoint for the treatment of a neurodegenerative disease. For example, adding a conclusion step which states ". . .and wherein an agent that potentiates CCE would be a potential agent for treating a neurodegenerative disorder." This is especially true with the limitation that the tests are performed in animal studies.

*Id.* Applicants respectfully disagree with the Examiner's assertions.

Section 2172.01 of the M.P.E.P., cited by the Examiner in support of this rejection, addresses unclaimed essential matter, and states that "a claim which fails to interrelate essential elements of the invention as defined by applicant(s) in the specification may be rejected under 35 U.S.C. 112, second paragraph for failure to point out and distinctly claim the invention." M.P.E.P. § 2172.01 (8<sup>th</sup> ed., Rev. May 2004). Applicants respectfully submit that the "conclusion step" that the Examiner alleges is

missing is already incorporated into presently presented independent claims 1 and 41, which recite "identifying said agent that potentiates CCE as a candidate agent for treating a neurodegenerative disease characterized by symptoms comprising amyloid aggregation or apoptotic neuronal cell death." In addition, independent claims 1 and 41 currently recite "testing said identified candidate agent in animal studies for parameters comprising toxicity and stability." Therefore, Applicants respectfully submit that there are no omitted steps, and no failure to interrelate essential elements of the claims.

Accordingly, the Examiner's grounds of rejection of claims 1-9 and 41 under 35 U.S.C. § 112, second paragraph, have been rendered moot. Applicants, therefore, respectfully request the Examiner to reconsider and withdraw this rejection.

***Rejections under 35 U.S.C. § 102***

Applicants thank the Examiner for withdrawing all of the rejections under 35 U.S.C. § 102. (See Office Action dated July 2, 2004, Section 5.)

***Rejections under 35 U.S.C. § 103***

Claim 1 has been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Berridge *et al.*, *Biochem. J.* 312: 1-11 (1995) ("Berridge"). (Office Action dated July 2, 2004, Section 6.) Applicants respectfully traverse this rejection.

In particular, the Examiner asserted that:

[i]t would have been obvious to one of ordinary skill in the art at the time of the present invention to have performed screening methods in animals since this data would provide more useful [?<sup>1</sup>] for the treatment of diseases than simply using cells in vitro. There would have been a

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<sup>1</sup> The Examiner appears to have omitted a word. From context, Applicants believe that the Examiner meant to write "useful information" or a similar phrase.

reasonable expectation of success for one of ordinary skill in the art to have used animal studies to screen for compounds affecting CCE since animal studies were well-known at the time of the present invention.

*Id.* Applicants respectfully disagree with these assertions.

Section 2143 of the M.P.E.P. sets forth the basic requirements for a *prima facie* showing of obviousness:

First, there must be some suggestion or motivation, whether in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference... must teach or suggest all the claim limitations.

M.P.E.P. § 2143. The M.P.E.P. further states that "[t]he teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure." *Id.* Applicants respectfully submit that there is an inconsistency in the Examiner's arguments during prosecution such that Berridge cannot render obvious the invention of claim 1.

The Examiner asserted in the most recent Office Action that, although Berridge does not teach testing in animal studies, "it would have been obvious to one of ordinary skill in the art at the time of the present invention to have performed screening methods<sup>[2]</sup> in animals since this data would provide more useful [information] for the treatment of diseases than simply using cells *in vitro*." (Office Action dated July 2, 2004, at page 4.) However, at page 6 of an earlier Office Action dated May 12, 2003, the Examiner acknowledged that Berridge "does not teach that CCE is linked to neurodegenerative diseases." Hence, if Berridge does not even teach that CCE is linked

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<sup>2</sup> Applicants point out that the claims recite "testing said identified candidate agent in animal studies for toxicity or stability."

to neurodegenerative diseases, then it certainly cannot follow that Berridge would suggest to one of ordinary skill in the art to test a candidate agent in animal studies for the Examiner's proffered reason that "this data would provide more useful [information] for the treatment of diseases."

The Examiner suggested that "animal studies were well-known at the time of the present invention." (Office Action at page 4.) Even assuming this to be the case, in order to support an obviousness rejection, it is necessary to consider the claimed invention as a whole. "In determining the differences between the prior art and the claims, the question under 35 U.S.C. § 103 is not whether the differences themselves would have been obvious, but whether the claimed invention as a whole would have been obvious." M.P.E.P. § 2141.02 (citations omitted) (emphasis in original). Therefore, just because animal studies *in general* were known does not render the claimed method, of which testing in animal studies is only one part, obvious over Berridge.

Thus, because Berridge fails to teach or suggest at least: 1) identifying a candidate agent for treating a neurodegenerative disease and 2) testing the identified candidate agent in animal studies, Berridge fails to render the claimed invention obvious. Accordingly, this rejection has been overcome or otherwise rendered moot, and Applicants respectfully request that the Examiner reconsider and withdraw the rejection.

Claim 1 has also been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Birnbaumer *et al.*, U.S. Patent No. 5, 932, 417 ("Birnbaumer") for the same reasons set forth with respect to Berridge. (Office Action dated July 2, 2004, Section 6.) Applicants respectfully traverse this rejection.

As with Berridge, at page 5 of the Office Action dated May 12, 2003, the Examiner acknowledged that Birnbaumer "does not teach that CCE is linked to neurodegenerative diseases." Since, as with Berridge, Birnbaumer does not even teach that CCE is linked to neurodegenerative diseases, it certainly cannot follow that Birnbaumer would suggest to one of ordinary skill in the art to test a candidate agent in animal studies for the Examiner's proffered reason that "this data would provide more useful [information] for the treatment of diseases." Again, the Examiner suggested that "animal studies were well-known at the time of the present invention." (Office Action at page 5.) However, as set forth above, merely because animal studies *in general* were known, this does not render the claimed method, of which testing in animal studies is only one part, obvious over Birnbaumer.

Thus, because Birnbaumer does not teach or suggest identifying a candidate agent for treating a neurodegenerative disease or testing the identified candidate agent in animal studies, Birnbaumer, in light of the knowledge generally available to one of ordinary skill in the art, does not teach or suggest all of the claim limitations, and does not render the claimed invention obvious. Accordingly, this rejection has been overcome or otherwise rendered moot, and Applicants respectfully request that the Examiner reconsider and withdraw the rejection.

***Conclusion***

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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